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ABSTRACT

Guidelines are presented which were developed to aid federal, state, and local agencies prepare regulations concerning the use of mentally retarded subjects in biomedical and pharmacological research projects. Guidelines are set forth for the following topic areas (sample subtopics in parentheses): the formation of a Professional Review Committee to monitor the conduct of research; the formation of a Committee on Legal and Ethical Protection; researchers and the research setting (qualifications, appropriate medical supervision); types of research (categories of biomedical and pharmacological research); informed consent (competent institutionalized mentally retarded individuals, elements of informed consent, coercion); withdrawal of consent; ongoing review; and enforcement mechanisms (prevention of abuses, sanctions). (CL)

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NUMBER 4

M.R. RESEARCH

GUIDELINES FOR BIOMEDICAL AND PHARMACOLOGICAL RESEARCH PROCEDURES AND THE PROTECTION OF HUMAN SUBJECTS IN RESIDENTIAL FACILITIES FOR MENTALLY RETARDED PERSONS

A MONOGRAPH SERIES PUBLISHED BY

THE RESEARCH ADVISORY COMMITTEE

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Clarity of writing and relevance to mental retardation are primary criteria which all manuscripts must possess in order to be considered for publication. Generally, technical reports of results of studies will not be suitable for submission. Articles which summarize large bodies of previously published research and which draw meaningful conclusions for the field would, however, be appropriate.

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Correspondence should be addressed to Chairman, Research Advisory Committee, NARC Research and Demonstration Institute, 2709 Avenue E East, Arlington, Texas 76011.

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FORWARD

This report is the product of a National Association for Retarded Citizens (NARC) task force charged with the development of safeguards and enforcement mechanisms for the protection of mentally retarded persons who participate in biomedical and pharmacological research studies while living in residential facilities. Thus, these guidelines do not encompass all research activities, e.g., behavioral research. Nor, for example, do they include research carried out using only medical records.

Earlier, the task force had drafted a resolution which was subseqeuently adopted by the delegate assembly of the National Association for Retarded Citizens' Annual Convention, October 23, 1975. The present guidelines and procedures were developed as part of the mandate of that resolution which appears below:

RESOLUTION #4

BIOMEDICAL[1] AND PHARMACOLOGICAL[2] RESEARCH ON MENTALLY RETARDED PERSONS 'N RESIDENTIAL FACILITIES

WHEREAS, one of the stated purposes of the National Assosiation for Retarded Citizens (NARC) is "to further the advancement of ameliorative and preventive study and research in the field of mental retardation," and

WHEREAS, NARC has had and continues to have commitment to this purpose, and

WHEREAS, the Congress and the Executive Branch of the federal government have made strides in addressing the problems of protecting the human and civil rights of mentally disabled persons, and

[1]Biomedical research, development and related activities means research, development or related activities involving biological study (including but not limited to medical or surgical procedures, withdrawal or removal of body tissue or fluid, administration of chemical substances or input of energy, deviation from normal diet or hygiene and manipulation or observation of bodily processes). Reference: Federal Register, Vol. 39, No. 169, Friday, August 23, 1974.

[2]Pharmacological research seeks to learn "whether or not a particular drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof and whether such drug is effective." Reference: Federal Food, Drug and Cosmetic Act, CH5, 505 (d) (i) (b).

WHEREAS, the application of newly developed biomedical procedures and pharmacological agents to human subjects needs to be studied before such procedures can be accepted for use by the general public, and

WHEREAS, there have been a number of abuses in biomedical and pharmacological research using mentally retarded persons as subjects and particularly mentally retarded persons living in institutions, and

WHEREAS, many institutionalized retarded persons neither comprehend the significance of such biomedical or pharmacological research nor understand the risks involved, nor the consequences it may have upon them as subjects, and

WHEREAS, institutionalized retarded citizens are unusually vulnerable to risk, because they may be physically delicate, have other handicapping conditions and may be unable to explain how they feel during an experiment, and because adequate mechanisms for the protection of their rights may be lacking, and

WHEREAS, mentally retarded persons have the same human and civil rights as all other persons, therefore

BE IT RESOLVED that no biomedical or pharmacological research shall be conducted in state operated or state licensed residential facilities for mentally retarded persons nor in any facility for mentally retarted persons which receives federal monies, until adequate and enforceable safeguards embodying the following principles are developed to protect participants in research in residential facilities for mentally retarded persons:

1) *Such research shall be conducted by scientifically qualified individuals in an adequately administered and equipped setting in which the participants shall be given appropriate medical supervision by a professionally qualified clinician, and*

2) *A scientifically qualified and competent reviewing body shall monitor the conduct of the research and the research project. This reviewing body shall be separate from the*

reviewing body described in subsection 5 (below) charged with protection of the rights of the participants. This reviewing body shall determine that there is no other appropriate population to participate in such research, and

3) *Such research shall be directed at the alleviation and/or prevention of mental retardation or shall have a reasonable expectation of direct therapeutic benefit to the participants, and*

4) *There shall be competent, voluntary and individual informed consent which is knowledgeable and autonomous and given by the individual, his parent or legal guardian without coercion or duress. For this purpose, legal guardian shall not constitute a government entity or an employee thereof which is directly involved in the care and treatment of the mentally retarded individual, and*

5) *A reviewing body which shall be independent of the researcher and institutional setting, such as a human rights review committee or a court of competent jurisdiction, shall have supervised, monitored, and assured that individual informed consent procedures have been fulfilled, and*

6) *The researchers, the institution or facility housing the participants and both of the reviewing bodies shall continuously monitor the research on an on-going basis, shall evaluate interim results as to possible changes in health or risk factors to the participants, shall monitor changes in or deviations from the original research protocol, and shall be responsible for initiating appropriate action in consequence of their findings, and*

7) *The rights of individuals not to participate or to withdraw from such research at any time and for any reason shall be fully respected and protected, and*

8) *Adequate enforcement measures shall exist for the protection of the participants.*

BE IT FURTHER RESOLVED that NARC develop specific guidelines and safeguards to effectuate the above policies. In developing these safeguards and guidelines, NARC shall address those abuses which have occurred in the past and

specifically enumerate safeguards which will ensure that such abuses shall not occur in the future.

BE IT FURTHER RESOLVED that the President of NARC shall call upon the U.S. Secretary of Health, Education and Welfare, and the Presidents of the State Member Units shall call upon the state governors, to effectuate this resolution and the specific NARC guidelines and safeguards.

BE IT FURTHER RESOLVED that each State Member Unit be responsible in its own state for action in conjunction with the appropriate bodies to review and ascertain the extent to which adequate safeguards and enforcement machinery are in effect and to seek suspension or prohibition of research in settings where the principles enunciated above are, or are likely to be, violated, and that NARC make available technical assistance compatible with its resources, on request from any State Member Unit engaging in such review.

BE IT FURTHER RESOLVED that this resolution shall be distributed to relevant federal and state agencies and private organizations.

BE IT FURTHER RESOLVED that this resolution supercedes that entitled "Human Medical Experimentation" adopted by the assembled delegates to the Anaheim Convention of the National Association for Retarded Citizens on November 3, 1973.

Task Force Composition

The task force was originally appointed by NARC President Marion P. Smith in April 1975. Upon his election as President of NARC the following October, Frank J. Menolascino, M.D., who had previously chaired the group, asked Karl Schmeidler, Esq., to become chairman. Other individuals participating on the task force were: John K. Sterrett, Ph.D.; Jack Gruenenfelder, Ph.D.; Ben N. Saltzman, M.D.; Eleanor S. Elkin; L. Steuart Brown; Jack G. May, Ph.D.; Julie Parsons; Rebecca Fitch, Esq.; and Ronald Neman, Ph.D.

INTRODUCTION

The past few years have witnessed a burgeoning interest in protection of the rights of many persons including minorities, children, women, physically handicapped persons, and institutionalized persons, including prisoners, mentally ill persons, and mentally retarded individuals. One of the many concerns which has been raised focuses on the appropriate conditions under which institutionalized persons may participate in research studies. This issue has been of particular interest to the National Association for Retarded Citizens because research, particularly biomedical and pharmacological research, has often been carried out in residential facilities for mentally retarded persons and has involved the use of residents as the subjects of such research.

The guidelines set forth in this document were developed to aid various federal, state and local agencies in the preparation of regulations concerning the use of mentally retarded subjects in biomedical and pharmacological research projects. NARC is strongly committed to the adoption of these guidelines and urges that they be written into legislation and regulations for this purpose. Some of the proposals set forth in this document can assist in dealing not only with the protection of research subjects but with the protection of residents from abuse in general. This is because problems encountered with research reflect a larger one, the conditions of institutionalization and the possibilities for abuse in institutions.

The guidelines mirror the Association's dual commitment of protecting mentally retarded persons from abuse, and at the same time encouraging research which bears significantly on mental retardation. These commitments were seen reflected in the forerunner of this document, the NARC Policy Statement on Research Ethics (October 30, 1973) which read in part that the nation's mentally retarded citizens, "...especially those in institutions, have frequently been subjects in medical and behavioral research. Their particular position in society and unusual vulnerability necessitates special ethical considerations for such research endeavors." The fundamental principle guiding the preparation of these guidelines was the development of mechanisms that will prevent abuse in the conduct of biomedical and pharmacological research. While sanctions or punishments may deter abuses, they cannot undo harm which has been done.

The primary focus then was on the development of means to stop and prevent abuse before, rather than after, it has occurred.

A second principle was the belief that the rights of research subjects require local monitoring. The failure of the Food and Drug Administration to monitor adequately drug research in several states underscores the need for local responsibility. Local review makes feasible continuous on-site inspection of the research facilities, face-to-face interviews with the participants and research staff and immediate intervention at the first indication that such action is needed.

A third principle has been that internal institutional monitoring of research on human subjects, while good and desirable, is insufficient. Employees of the institution are apt to have a conflict of interest and to be subject to the normal pressures, even if unintended, of continuing association with superiors, peers, and associates.

A fourth principle has been that the scientific and medical evaluations of a research proposal are different from decisions regarding human rights. Consequently, different kinds of bodies are needed for these two kinds of decisions. For example, ascertaining the risk entailed by a research procedure is a scientific-medical decision, but judging the procedures for informed consent is not.

In accordance with these principles, two distinct kinds of decision-making bodies are proposed: a professional review committee and a committee on legal and ethical protection. The professional review committee would be statewide. A specific committee on legal and ethical protection would exist both statewide and for each institution or region. These kinds of review bodies were first proposed in an earlier document entitled Guidelines for the Use of Behavioral Procedures in State Programs for Retarded Persons (NARC, 1975). Descriptions of these committees and their responsibilities follow in the next sections.

1 *Professional Review Committee*

A scientifically qualified and competent reviewing body shall monitor the conduct of the research and the research project. This reviewing body shall be separate from the reviewing body charged with protection of the rights of the participants. This reviewing body shall determine that there is no other appropriate population to participate in such research.

Within each state, a professional review committee (PRC) shall be established with adequate staff support and having authority and responsibility for the scientific review of biomedical and pharmacological research having as subjects individuals who live in residential facilities for mentally retarded persons. Before initiating any research in state operated and/or licensed facilities, researchers must receive written approval from the PRC. The PRC shall prepare a publicly available report of each review, stating findings, conclusions and the basis of the approval of each project. In addition, the committee shall review the conduct of the research during the progress of the project based on reports from the committee on legal and ethical protection described in the next chapter, reports from the researcher and, if deemed advisable, by on-site inspection. The committee shall be responsible for preparing an annual report summarizing the status of all projects reviewed and their disposition, including the findings of projects that have been approved and completed. A brief summary of findings or results from each completed project shall be included. The PRC shall have sufficient staff to carry out its responsibilities.

If at any time during the course of a research project, harm or increased risk to participants occurs or if unapproved deviations from the approved protocol occur, the committee shall be authorized to investigate the project directly and, if deemed appropriate, shall order a halt to the project on a temporary or permanent basis.

1.1 Review of Project Proposal

The PRC shall review each written proposal for biomedical and pharmacological research to be conducted in residential

facilities for mentally retarded persons (desirably within one month and no later than two months from the time the proposal is received) with regard to the following criteria:

1.1.1 Need for the research. Either of two kinds of needs may be regarded as legitimate pursuits of research to be conducted in facilities for mentally retarded persons--the discovery of knowledge directly bearing on the alleviation and/or prevention of mental retardation or intervention providing a reasonable expectation of direct therapeutic benefit to the participants and to other similar to them.

1.1.2 Methodological adequacy. The proposal shall be reviewed with respect to all relevant aspects of scientific methodology. This review shall include but not be limited to appropriate sampling procedures, experimental design, laboratory technology, control of variables and statistical analyses. The hypotheses shall be examined for clarity and completeness.

1.1.3 Redundancy with other projects. The PRC shall examine the proposal to determine if the scientific questions or hypotheses are adequately addressed in other research studies.

1.1.4 Scientific and theoretical justification for the research. The proposal shall spell out the scientific or theoretical basis, and the documented professional and scientific literature underlying the research to be carried out.

1.1.5 Competence of the researcher(s). The researcher(s) shall have demonstrated competence for the specific problem area proposed for the study and preferably for research involving mentally retarded persons. They shall be competent to conduct all scientific procedures required by the methodology. Further, the PRC shall determine that the researcher(s) have adequate medical support to conduct biomedical or pharmacological treatment or intervention methodologies. The competence of staff under the scientific researchers to carry out their assigned responsibilities shall be reviewed. The proposal shall clearly specify any training of staff that will be needed.

1.1.6 Funding sufficiency. The PRC shall assure that sufficient funds will be provided to carry out the project in the manner described in the proposal, including an adequate project staff required for the conduct of the research, analysis of the data and

reporting the results to subjects, advocates, their parents or guardians, the scientific community and the public. The researcher may obtain provisional PRC review prior to seeking funding for his or her proposal.

1.1.7 Risks and potential benefits. The PRC shall make a listing of all potential risks to the subjects which may result from the proposed research and an evaluation of the potential positive outcomes in terms of direct therapeutic benefit or in terms of the acquisition of knowledge pertaining to the alleviation and/or prevention of mental retardation. Only research in which reasonably expected potential benefits substantially outweigh potential risks shall be approved for initiation [see also 4.5 and 4.6].

1.1.8 Appropriate subject population. Approval of any research project shall be dependent upon a determination that no other appropriate subject population is available. The ease of conducting research in an institution shall not be considered an appropriate reason for determining that the proposed institutional population is the only available appropriate population [see also 4.3].

1.1.9 Adequacy of consent information. The PRC shall determine that the risks, benefits and procedures described in the proposed informed consent statement by the investigator correspond accurately with those the PRC has independently concluded to be associated with the proposed experimental procedures [see also section 5].

1.1.10 In the event that the PRC lacks sufficient expertise in the subject area of the proposed research, it shall be authorized to obtain sufficient outside reviews to make a clear determination of the proposal's disposition.

1.2 Report on Proposal Review

The PRC shall prepare a public report which addresses each of the issues above and which shall be distributed to the governor, the researcher and an appropriate committee on legal and ethical protection within the state. In its report, the PRC shall make a determination that a) the proposal is cleared for implementation, b) the proposal requires modification or further review, or c) the proposal is rejected.

1.3 Ongoing Review

A periodic report shall be prepared for the PRC by the research project staff. The PRC shall state in its initial clearance report the frequency and form of these research reports. It is anticipated that these requirements will vary according to the nature of the ongoing research, the degree of risk and other variables which the committee feels are appropriate. In addition to reviewing these reports, the committee shall review routinely reports from the investigator on the health status of subjects involved and of any and all untoward reactions among participants occurring during the study. As a condition of approval of the research proposal, the researcher shall agree to provide the PRC with a written report of results and a summary following completion of the study.

In addition, the PRC shall have a number of specific responsibilities related to a federal registry of research projects, described in section 8.1.3 of this document.

1.4 Committee Composition

The committee shall consist of several persons of demonstrated and recognized competence in diverse fields such as medicine, pharmacology, behavioral sciences, biomedical sciences, philosophy of science and bioethics. Such persons should be able to devote several working days per month if needed to PRC functions. Each member should be appointed for a fixed term by the state governor based on recommendations from state level consumer representatives and consumer groups whose primary concern is mental retardation, professional groups, universities, professional associations, and editorial boards of professional journals. The PRC shall be authorized and provided sufficient support to seek the assistance of professional consultation when deemed necessary or appropriate in carrying out its functions. The PRC shall be given necessary staff to carry out its functions.

Prior to the appointment, the number of members, the length of terms and rotation mechanisms along with the compensation and budget necessary (from state appropriations) for the committee to function should be clearly established.

In large states or in states where large amounts of research are being carried out, it may be necessary to have regional professional review committees. This would permit reviewers to attend meetings more easily and make site visits when called for.

2 *Committee on Legal and Ethical Protection*

> A reviewing body which shall be independent of the professional review committee, the researcher, and institutional setting, such as a human rights review committee, or a court of competent jurisdiction shall have supervised, monitored and assured that individual informed consent procedures have been fulfilled.

Committees on legal and ethical protection (CLEP), established at a state level and on a regional or local basis (e.g., in conjunction with major residential facilities), will assure that proposed biomedical and pharmacological research shall employ appropriate procedures for individual informed consent of potential participants, will monitor the conduct of research with respect to protection of the rights of the participants and will intervene in cases where the rights of the participants are in jeopardy or abused.[1] Intervention may be considered by the CLEP at its own initiative or at the request of concerned parties, including parents and state and local Associations for Retarded Citizens. Prior to the initiation of a research project, written approval by the local CLEP must be given. Decisions of the local CLEPs may be appealed to the state CLEP. The latter may review local CLEP decisions and make a final determination as to whether approval should be given or denied to the initiation of a project.

2.1 Composition of CLEPs

State and local CLEPs shall be composed of several members, all of whom shall be unaffiliated with the research project, the state department or the agency responsible for residential

[1]The CLEP may be part of the state Human Rights or Developmental Disability Protection and Advocacy Agency, providing it meets the requirements of these guidelines.

facilities, the institution in which the research shall be conducted or publicly supported service delivery systems. Members shall be appointed by the state governor for a fixed term. Terms should be staggered and provisions made for the rotation of members. At least one member each should be appointed upon the advice of: a) consumers or representatives of consumer groups; b) the state bar association; c) the state medical association; and d) an active behavioral science association, such as the state psychological or state educational associations. Remaining members should be consumers or representatives of consumer groups whose primary interest is representing mentally retarded persons. Provisions for adequate staff and for reimbursement of CLEP members (from state appropriations) shall be made for expenses incurred in carrying out their duties.

2.2 Functions of Local CLEPs

CLEP approval of projects shall involve two separate stages. The first includes a) evaluation of plans and procedures for securing informed consent, and b) permission to select subjects. The second evaluates whether the consent obtained was, in fact, informed and met criteria set forth in section 5.10. Other functions shall include periodic site visits and the receipt and investigation of complaints.

2.2.1 Proposal review. Local CLEPs shall (desirably within one month and no later than two months from the time the proposal is received from the PRC) review biomedical and pharmacological research proposals which have been approved by a PRC to determine if provisions for protection of the rights and welfare of the subjects are specifically adequate with regard to a) informed consent procedures, b) sufficiency of human and other resources necessary to provide appropriate physical and mental health care and to monitor the health status of potential subjects, and c) whether the standards outlined in these guidelines are met. The CLEP shall prepare a written report on its review and shall be authorized to grant or deny permission for the research to proceed with the selection of subjects.

2.2.2 Research participants. The CLEP shall determine that persons selected to participate in the research or their guardians shall have been informed of the proposed procedures in a manner sufficiently clear that they can make a decision whether or

not to participate based on their individual best interests and wishes. More specific details on informed consent procedures are given in Section 5 of these guidelines.

Initiation of the experimental procedures shall require prior written approval from the CLEP that all necessary and sufficient aspects of the informed consent procedures have been completed.

2.2.3 Periodic visits. The CLEP shall conduct periodic visits and on-site inspections of facilities or programs within their respective regions to ensure continued familiarity with their operations and to ensure that the facilities are conforming to the required standards and that no unauthorized research is occurring. The CLEP, selected members, or its representatives or staff shall have direct access to any place in the institution at any time and to all records excepting pre-existing records that are confidential by state statutes. The CLEP shall be charged with the strict maintenance of confidentiality of any and all individual information it may obtain while carrying out its functions.

2.2.4 The CLEP shall also receive complaints regarding research programs when lodged by participants, parents, staff, public officials, and members of the press or the public. The CLEP shall have authority to investigate the conduct of the research regarding such complaints. If the CLEP finds evidence of abuse in any research program, it shall be authorized to order a halt to the program and shall immediately notify the state CLEP and the state PRC.

2.3 Investigational Inquiry

In the event that increased morbidity or mortalities occur among participants in research, the CLEP shall immediately begin an investigational inquiry. Increased morbidity may be reflected in the occurrence of isolated events of serious illnesses or injuries or in a general increase in the frequency with which participants display symptoms, illness or injury. In all cases where deaths occur, the CLEP shall receive an autopsy report to determine if the death is related to the research procedures. In carrying out this inquiry, the CLEP shall be authorized to obtain the services of outside individuals, including members, staff or consultants to the PRC. The PRC may be directly involved

in the investigation where questions about methodology are involved. The CLEP shall make a written report of its findings and conclusions if violations of safeguards or approved procedures have occurred. If the research appears to be causally related, a report shall be prepared for the PRC. At the discretion of the CLEP, the research may be temporarily suspended pending a determination by the PRC whether the suspicion of a causal connection is warranted.

If there is reason to believe criminal actions or violations of professional or civil codes have occurred, the CLEP may seek appropriate legal action. If the research is found to be causally related to the increased morbidity or death, a report to the research registry [see section 8.1.3] shall be made by the PRC.

2.4 Other Duties

While the specific CLEP functions outlined in these guidelines pertain to biomedical and pharmacological research, in some states it may be feasible to assign additional responsibilities to the CLEP. For example, the Guidelines for the Use of Behavioral Procedures in State Programs for Retarded Persons enumerates roles for a CLEP in the supervision of the application of behavioral procedures in residential facilities. The CLEPs as constituted in these guidelines can ideally serve a number of other protective functions needed in state facilities.

2.5 Functions of State CLEPs

Specific functions of state level CLEPs shall include the following:

2.5.1 Standards for informed consent. The state CLEP shall develop detailed standards for informed consent which shall be complied with prior to the initiation of any research in a state licensed residential facility. Such standards should include consideration of points discussed in section 5.10 of these guidelines.

2.5.2 Appeal process. The state CLEP shall hear appeals from either researchers or members of the public relating to decisions made by local CLEPs. The state CLEP shall be authorized to

review in entirety a research proposal not approved by a local CLEP and to maki a determination as to whether or not the proposed research should proceed. Similarly, the state CLEP shall review appeals from members of the public who oppose initiation of a research project which has received approval from a local CLEP.

2.5.3 Emergency powers. The state CLEP, in conjunction with the local CLEPs, shall be vested with emergency powers to intervene in crisis or emergency situations emanating from an ongoing research project within a residential facility.

2.5.4 Legal intervention. The state CLEP may, in conjunction with the local CLEP, seek the initiation of legal action in cases of: a) marked deviations from approved procedures; or b) direct abuse or violation of the legal rights of the subject participants. If the guidelines for research are violated, the CLEP may seek an injunction to prevent the researcher and sponsors from continuing the research. If an investigation proves that a willful violation of established safeguards has occurred, the CLEP may ask the proper state agency e.g., the attorney general's office, to bring criminal or other appropriate proceedings.

3 *Researchers and the Research Setting*

Such research shall be conducted by scientifically qualified individuals in an adequately administered and equipped setting in which the participants shall be given appropriate medical supervision by a professionally qualified clinician.

3.1 Scientifically Qualified Individuals

Scientifically qualified individuals are persons who by their training, education and experience have acquired the skills and knowledge necessary to direct and conduct biomedical and pharmacological research studies and to analyze and interpret the results in a meaningful manner. Such individuals should have advanced degrees in scientific disciplines such as medicine, biomedical sciences and behavioral sciences, be certified and licensed by state level examination boards where appropriate and have demonstrated their competence by published research in the area of their specialization.

3.2 Adequately Administered and Equipped Setting

The facility in which the research is to be conducted shall have the equipment and personnel necessary to supervise the health care status of all individuals taking part in the research project. In determining that the level of personnel and facilities are adequate, care must be taken to assure that the needs of other residents will not be compromised by diverting normally available resources to participants in research projects. In order for a residential facility to be certified as an appropriate facility, it must have received accreditation by the Accreditation Council for Services for Mentally Retarded and Other Developmentally Disabled Persons (AC/MR-DD).

3.3 Appropriate Medical Supervision for Biomedical and Pharmacological Research

The health status of individuals taking part in biomedical or pharmacological research shall be subjected to constant scrutiny by the medical staff of the facility wherein the research is taking place. This supervision shall take place by trained medical personnel under the direction of a licensed physician. The level of care and supervision required will be dependent upon the nature of the research and the degree of risk and discomfort which is involved. Responsibility for such medical supervision shall be above and beyond the routine health care maintenance program which is carried out by the facility. The frequency of supervision for a particular study (e.g., hourly, daily, twice a week) shall be spelled out by the PRC in its report to the CLEP. Written reports on the type of ongoing monitoring and the information gained shall be maintained for each participant by the researcher. These written reports shall be available for inspection by the CLEP or their authorized representative upon request.

3.4 Professionally Qualified Clinicians

Medical supervision of the participants shall be the responsibility of a licensed physician and other medical personnel under the supervision of that physician. The other personnel may include licensed physicians, registered nurses, and other licensed medical personnel. The treating physician who is responsible for a resident's medical care shall not be associated with the

research project in any formal way, nor receive any form or remuneration from the research project for duties carried out in supervision of the research participants. However, the researcher may hire special additional medical specialists to oversee the health of the participants or to serve as consultants to the treating physicians. These specialists, however, shall not be permitted to serve as substitutes for a qualified treating physician independent of the research project.

4 *Types of Research*

Such research shall be directed at the alieviation and/or prevention of mental retardation or shall have a reasonable expectation of direct therapeutic benefit to the participants.

4.1 Research

Research is the application of scientific methodology, typically including the testing of hypotheses by noting the relationship, if any, of dependent variables to independent variables and applying suitable statistical procedures. Research may involve the use of scientifically validated procedures or techniques for the purpose of gathering data or new information, or the use of a scientifically unvalidated procedure or technique to test its safety and efficacy. Both types of research must be conducted pursuant to a research proposal based upon scientific methodology.

Biomedical and pharmacological research proposals which meet the requirements of the NARC resolution and these guidelines shall be permitted in institutions for mentally retarded persons. It shall be the responsibility of the PRCs and CLEPs to evaluate all proposals to determine whether they conform with these standards.

4.2 Biomedical and Pharmacological Research with Direct Therapeutic Benefit

Direct therapeutic benefit means that the physical and/or mental health of the individual participants--and eventually other retarded persons--shall have a reasonable expectation of improvement as a consequence of the experimental procedures or that their ability to cope with their environment shall be improved. Such

benefit may accrue as a result of amelioration of the chronic handicapping consequences of mental retardation, intervention in biochemical processes which produce or maintain the condition or increasing the extent to which an individual is capable of exerting control over his other functions. Therapeutic benefit also pertains to medical or other procedures not directly related to the individual's condition with respect to mental retardation but resulting in an improvement in the participant's health status or the prevention of deterioration of the health status.

Biomedical and pharmacological research with potential direct therapeutic benefit should not be confused with either accepted practice or experimentation, both of which may result in therapeutic benefit.

Accepted practices refer to treatments that have already undergone research, e.g., are scientifically validated and are approved as safe and effective for the purposes for which they are being administered. Mere acceptance by the professional medical community, of course, is not scientific validation. That a procedure is in common use or endorsed by some professionals does not constitute sufficient evidence that the treatment is no longer an experimental one.

An experimental treatment or procedure is one which has been subject to some study and has been authorized for further study (conducted according to a research plan). Such treatments have not been licensed for general public use, however.

Experimentation is the application of unvalidated procedures to subjects with the expectation that they may have some influence on the subjects, and differs from the situation in which the patient and physician seek alternatives among accepted treatments. Experimentation should not be conducted in a residential facility.

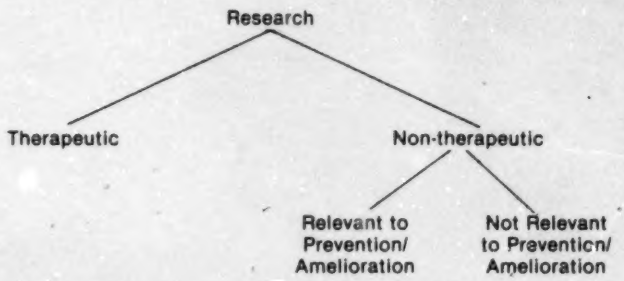
4.3 Research without Direct Therapeutic Benefit

Research which is non-therapeutic in nature must be directed toward the alleviation or prevention of mental retardation. No other type of non-therapeutic biomedical or pharmacological research shall be permitted in institutions for mentally retarded

persons. In determining that the research protocol is appropriate, a determination must be made not only that the research is related to mental retardation but that the subject population is the only appropriate population. Thus, for example, research on a meningitis vaccine would fit the criterion of mental retardation related research; however, it would not meet the second criterion since this type of research could appropriately be done on non-institutional populations.

4.4 Categories of Biomedical and Pharmacological Research

Formal research projects can be divided into two broad categories: those with potential direct therapeutic benefit to the participants and those which do not have such potential benefit. Non-therapeutic research can also be subdivided into research which has relevance to the prevention and/or amelioration of mental retardation and that which does not. This breakdown is illustrated below:

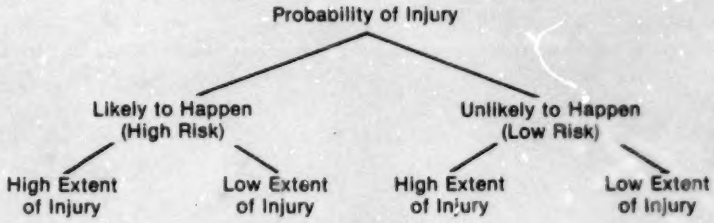


These categories will be useful in a further discussion below of types of research to be permitted in residential facilities for mentally retarded persons.

4.5 Risk

Research can pose risks to participants which may vary in probability of occurrence and in extent of injury (e.g., physical damage, psychological trauma, or regression of health status). Four broad descriptive categories of risk can thus be formulated, including research with a) high probability of risk and high injury potential; b) high probability of risk and low injury potential; c) low probability of risk and high injury potential; and d) low pro-

bability of risk and low injury potential. Risk probability refers to the liklihood that injury or harm will occur, regardless of the extent of the injury or harm. Extent of injury refers to types of consequences which may inpinge upon the subject regardless of the frequency or likelihood with which they may occur. The four categories which result do not, of course, reflect precisely defined, mutually exclusive situations, since in actuality both the probability of harm and the extent of injury vary widely. The four categories reflect relative degrees of risk and injury and provide a basis for deliberation and review by PRCs and CLEPs. The four categories are illustrated below:


Probability of Injury
Likely to Happen (High Risk)
Unlikely to Happen (Low Risk)
High Extent of Injury
Low Extent of Injury
High Extent of Injury
Low Extent of Injury

4.6 Risk versus types of Biomedical and Pharamcological Research

The type of biomedical and pharmacological research which shall be permitted within residential facilities for mentally retarded persons and the risk involved were examined by the task force with respect to two other variables, individual capacity and extent of coercion (see also sections 5.3 and 5.4). The framework for this review is the table below which combines risks and types of research.

Permissable research

Permissable research if potential benefits outweigh risks

Prohibited research

Probability	Types of Research		
	Therapeutic	Non-Therapeutic	
		Prevention/ Alleviation	Non-Prevention/ Non-Alleviation
High Risk (likely to happen) High extent of injury	1	5	9
High Risk (likely to happen) Low extent of injury	2	6	10
Low Risk (unlikely to happen) High extent of injury	3	7	11
Low Risk (unlikely to happen) Low extent of injury	4	8	12

The more darkly shaded portions of the table,boxes 5, 7, and 9-12,indicate circumstances under which no biomedical and pharmacological research shall be permitted in residential facilities for mentally retarded persons. This includes research that is neither therapeutic to the individual nor relevant to the prevention or alleviation of mental retardation. All non-therapeutic research posing serious potential injury to the participants, even where the probability of risk is low, shall be prohibited. Any proposed biomedical and pharmacological research which has neither potential direct therapeutic benefit to the participants nor relevance for the prevention or amelioration of mental retardation shall automatically be rejected by the PRC.

Non-therapeutic biomedical and pharmacological research which is preventative or ameliorative in nature but which poses

severe hazards, danger, injury or harm to the subjects shall not be permitted, even if the probability of occurrence of harm is low. Any non-therapeutic preventative or ameliorative biomedical and pharmacological research proposal which poses serious possible harm or injury shall automatically be rejected by the PRC without consideration of the possible merits inherent in the proposal.

Biomedical and pharmacological research which has potential direct therapeutic benefit to the participants and to others similar to them can generally be regarded as appropriate for consideration by the PRC and subsequently by the CLEP. However, research with a high extent of injury, even if the injury is unlikely to happen, shall only be carried out if the benefits are very high. In all biomedical and pharmacological research to be carried out in residential facilities for mentally retarded persons, potential benefits shall substantially outweigh the possible risks involved.

5 ***Informed Consent***

There shall be competent, voluntary and individual informed consent which is knowledgeable and autonomous and given by the individual, his parent or legal guardian without coercion or duress. For this purpose, legal guardian shall not constitute a government entity or an employee thereof which is directly involved in the care and treatment of the mentally retarded individual.

5.1 Prior to participation in any approved research project, each individual or, in limited circumstances defined below, the individual's parent, legal guardian or the CLEP must give voluntary informed consent to such participation. No individual shall participate in any research project unless this requirement is met for that individual.

While an exhaustive exploration of the subject of informed consent is not attempted in these guidelines, a number of specific issues are reviewed relating to: a) the accuracy and clarity of the description of the risks and benefits involved; b) the capacity of the individual to understand and comprehend the information which was supplied concerning the risks and benefits; c) con-

siderations with respect to problems in securing free and voluntary consent from institutionalized individuals; d) the circumstances under which substitute consent is appropriate and the procedures which should be followed in securing such consent; and e) the amount of information that should be supplied persons asked to participate in the research prior to their giving consent.

The procedures outlined below apply to formal research projects which are conducted pursuant to a research proposal which has been approved by the PRC and CLEP.

5.2 Competent Institutionalized Mentally Retarded Individuals

Competent mentally retarded individuals may agree or refuse to serve as subjects in research programs which have been approved by the PRC and CLEP. Whether the individual is competent to understand the risks, benefits and procedures involved in a research experiment depends both upon the capacity of the person and the complexity of the research experiment. An individual may have the capacity to understand what participation in one experiment involves yet be incapable of fully comprehending another experiment. For this reason, competency must be determined on an individual, case-by-case basis for each research project [see also section 5.9]. In making such determinations, the CLEP shall use all available consultive resources, including professional and direct care personnel in the facility who are personally knowledgeable about the proposed participants.

5.3 Incompetent Institutionalized Mentally Retarded Individuals with a Parent or Legal Guardian

In the case of an incompetent individual[1] who has a parent or has a legal guardian[2], substitute consent may be given on behalf of that individual by his or her parent or legal guardian for certain types of research, those illustrated in blocks 1-4, 6 and 8 on the chart in section 4.6[3]. Participation of incompetent individuals

[1]This is not necessarily a legally incompetent person but a person incompetent for informed consent on a particular research project.

[2]In this and subsequent references to legal guardians, the legal guardians may not be a governmental entity or an employee thereof which is responsible for the care and treatment of mentally retarded persons. An employee of a residential facility, for example, even though he may be the superintendent and the legal guardian of the resident, may not give substitute consent to participate in a research project.

[3]A number of legal issues surround the concept of substitute consent and there is disagreement whether substitute or vicarious consent is valid. This issue remains one which may eventually be settled by the courts.

shall be limited to research projects which are directly therapeutic or, if non-therapeutic, represent minimal risk having low extent of injury potential to the participant and which are related to the alleviation and prevention of mental retardation. Where a parent or legal guardian gives substitute consent, it shall be the responsibility of the CLEP to determine if the parent was fully informed and whether the parent or guardian was acting under coercion.

Since in some ways, it will be more difficult to determine the adequacy of consent given by retarded individuals judged competent to do so than to determine the adequacy of substitute consent, it is possible that subject selection could become biased by excluding from consideration those retarded persons who are considered competent. This is undesirable since such persons stand to gain from potential benefits of research just as do their non-competent peers. Thus, a research project should not exclude retarded individuals able to give informed consent and seek those unable to give it for ease of selection of subjects.

5.4 Incompetent Institutionalized Mentally Retarded Persons Who Lack Parents or Legal Guardians [see also section 4.6]

When an individual lacks a parent or legal guardian, the only type of research that individual may participate in is research with direct therapeutic benefit. Such individuals shall not be considered appropriate research subjects for non-therapeutic research.[1]

In instances where such an individual without parents or a suitable legal guardian is sought as a participant in a therapeutic research experiment, the CLEP shall be vested with the responsibility for giving or refusing consent. In such a case, the CLEP shall appoint an advocate to act upon the behalf of the institutionalized individual in gathering information and making a recommendation to the CLEP. These advocates shall be appointed from a specially designated pool of persons who have demonstrated an interest in the rights of mentally retarded persons and who are willing and able to devote the necessary time to their responsibilities. Such advocates need not be

[1]In extremely rare instances of non-therapeutic research involving minimal risk to the subject and the subject represents some unique, "one of a kind," or extremely rare individual, the CLEP, with special supervision, may wish to consider the participation of such an individual. However, all the protective mechanisms described in section 5.4 should be employed in the event of such participation.

attorneys. The decision whether or not to allow such an individual to participate in the research, however, shall rest with the CLEP. In the event that the recommendations of the advocate and the CLEP differ, the advocate may appeal to the state CLEP to review the decision or seek redress in a court of appropriate jurisdiction.

5.5 Responsibility of the CLEP to Determine if Voluntary Informed Consent has Been Given

The CLEP has the responsibility for reviewing all decisions to participate in research projects in order to determine whether appropriate informed consent has been given.

5.6 Competent Individuals

The CLEP or a panel of three or more CLEP members including a consumer representative shall interview each potential research subject to determine whether a) the individual received all necessary information with respect to the risks, benefits and procedures involved, b) had the capacity to understand the information which was given, and c) was influenced in his or her decision by any form of coercion, intended or otherwise. In interviewing the potential research subjects, the CLEP members shall ask the individuals to explain what the experiment consists of, the risk and benefit and why the individual has chosen to participate. Questions which elicit "yes" or "no" responses are not generally useful for this purpose.

5.7 Incompetent Persons with Parents or Legal Guardians

Where an incompetent individual having a parent or legal guardian is a potential research participant, the CLEP shall have responsibility for contacting the parent or legal guardian of such individual and determining whether he or she a) has been fully informed with respect to the research proposal; b) understands the information which was given; and c) is acting freely and voluntarily without being subjected to coercion.

5.8 Elements of Informed Consent

An individual may be considered to have given competent, voluntary informed consent when that individual:

5.8.1 Has the capacity to understand the risk, benefits and procedures with respect to the project he or she is asked to engage in.

5.8.2 Has been given sufficient information to understand the risk, benefits and procedures.

5.8.3 Is acting of his or her own free volition without undue coercive influence.

5.9 Capacity

Competency to consent to participate in a study is relative rather than absolute. It cannot be clearly related to any existing quantified index of cognitive or social competence (such as an intelligence or social quotient). Potential subjects, including persons of normal intelligence, may be competent to participate in some studies and not in others. It is, therefore, necessary to question individually each potential research participant or the person giving substitute consent on behalf of that individual to determine that the consenter clearly understands the procedures in which he is to participate and the potential consequences of his participation.

5.10 Adequate Information

The following list provides examples of the type of information and communication which is necessary to inform adequately a participant or the individual giving substitute consent.

5.10.1 Why was the particular subject chosen?

5.10.2 With whom will the subject interact during the course of the experiment, including the research personnel and other subjects?

5.10.3 When and where will the research be done?

5.10.4 How often will the procedures be repeated?

5.10.5 An explanation of the time span of the project and the amount of time the subject will be needed.

5.10.6 A statement of the overall purpose of the research and possible results.

5.10.7 The role of the subject. A full explanation of the procedures to be followed including an identification of those which are experimental.

5.10.8 A full description of the attendant discomforts and risks. No information about risks or discomforts may be withheld.

5.10.9 A full description of the benefits the subject may expect, including kinds of payment, if any.

5.10.10 A full and fair disclosure of appropriate alternative procedures which might be advantageous to the subject.

5.10.11 An offer to answer any inquiries concerning the procedures.

5.10.12 An offer to provide the treatment at the end of the project if it is proven beneficial and the subject does not receive it during the study.

5.10.13 Provision of outside independent consultation to the decision maker at his or her request.

5.10.14 An instruction that the subject or the subject's parents or legal guardians may withdraw consent and discontinue the subject's participation in a project or activity at any time.

All the foregoing must be communicated in an easily comprehensible form.

In all double blind studies where some persons receive treatment and some do not, subjects must be informed at some point in the research or at its conclusion whether they were in an experimental or control group. Ordinarily, subjects should be informed beforehand of the double blind nature of the study and that *they will not be told during the study which treatment, experimental or control, they will receive.* Where the investigator clearly spells out the need for an exception, i.e., cases in which knowledge of

the double blind design may confound the results, and both the PRC and CLEP approve, this information may be withheld until the end of the study. In all cases, if a treatment being studied proves beneficial or useful, subjects must be informed as to how they may obtain the treatment.

5.11 Coercion

Coercion refers to influences upon potential participants, their parents or legal guardians which may interfere with their free and voluntary choice to participate or not to participate in a research project. The decision to take part in an experiment as a subject should reflect the participant's wishes or those of his parents or guardian, not the wishes of other persons. Coercion can take two general forms, "the stick," where punitive or negative consequences are implied or made explicit for refusal, and "the carrot," where positive rewards for participation--other than the benefits of the study itself--are implied or made explicit. Some descriptions of coercion follow.

5.11.1 Manipulation of services. This form of coercion makes participation in a project a prerequisite for the receipt of services or threatens the withdrawal or reduction in level of services if individuals do not choose to participate. Such coercion may include contingent admission to residential facilities, receipt of appropriate medical services, placement in special additional programs, promises of a special consideration such as preferential selection for and the receipt of future planned expanded or improved services. If the CLEP finds that this form of coercion is being used, it shall terminate the research project.

5.11.2 Interpersonal manipulation. Potential participants may be given the impression that they will be more "liked," valued or desirable persons in the eyes of institutional administrators or staff members if they participate or that they will fall into the personal displeasure of and will disappoint administrators and staff of the facility if they do not participate. For example, subjects should not be told that a decision not to participate will impede the progress of science. If the CLEP finds that these or similar forms of coercion are being used, it shall prohibit the participation of any such coerced potential subjects in the research project and/or terminate the research project.

5.11.3 Payment of participants. The offering of financial compensation or other payment as inducement for persons to participate in research is a commonly used technique in a wide variety of settings. Residents of facilities for mentally retarded persons should be compensated for their time spent in research projects to the same extent that persons who are not in residential facilities are typically compensated.

5.11.4 Target of coercion. Both the potential subjects as well as their parents, advocates and guardians may be the focus of coercion. Particularly in cases where substitute consent must be obtained, the party who will give consent, i.e., parent, guardian, or advocate, may be equally the subject of coercion; for example, admission or continued placement in the institution may be contingent upon a parent giving approval for his or her child to participate in a research program or the amounts being charged for residential placement may be varied according to whether approval is given to take part in research studies.

6 *Withdrawal of Consent*

The rights of individuals not to participate or to withdraw from such research at any time and for any reason shall be fully respected and protected.

6.1 Competent Mentally Retarded Individuals

Individuals who have been determined to be capable of giving informed consent on their own behalf may withdraw from any research project, therapeutic or non-therapeutic, at any time for any reason.

6.2 Incompetent Individuals

6.2.1 Withdrawal by the parent, legal guardian or CLEP. Where a parent or legal guardian or, in cases in which none exists, the CLEP has given consent for an individual to participate in a therapeutic or non-therapeutic project, such individuals shall have the option to withdraw their consent at any time during the research project. Prior to withdrawal, such persons shall be fully

informed of any risks e.g., loss of gains made or benefits received from the experimental procedures to the subject which may result from premature withdrawal from the program.

6.2.2 Withdrawal by incompetent individual. Where an incompetent individual indicates that he or she wishes to withdraw from a non-therapeutic research project, that individual shall be permitted to withdraw at any time. In cases of research projects having potential direct therapeutic benefit, or where risks may attend premature withdrawal, the parent or legal guardian must agree to the withdrawal, or if none exist, the CLEP must agree.

The CLEP shall maintain periodic contact with the participants to ascertain whether they remain willing to continue in the activity and provide for the withdrawal of any participants who wish to do so. The CLEP shall, of course, guard against giving participants an impression that they either should or should not wish to continue or withdraw from the research. The CLEP shall also be authorized to terminate, by court proceedings if necessary, participation of one or more participants with or without their consent where conditions warrant.

7 On-Going Review

The researchers, the institution or facility housing the participants and both of the reviewing bodies shall continuously monitor the research on an on-going basis, shall evaluate interim results as to possible changes in health or risk factors to the participants, shall monitor changes in or deviations from the original research protocol, and shall be responsible for initiating appropriate action in consequence of their findings.

7.1 On-Going Review of the Research

The frequency and degree of detail involved in reviewing the health status of the subjects of the research shall be specified by the PRCs and CLEPs, acting with the assistance of necessary medical consultation. Projects in which the relative degree of risk or injury is high shall correspondingly require high supervision of the health status of participants. There shall be periodic information to participants, parents and guardians and the PRC and appropriate CLEPs regarding the status of the research and participants. At the same time, physicians charged with the

medical supervision of participants will be responsible for immediately reporting changes in the health status of participants if such changes occur between regular reports to the CLEPs. During the course of the project, CLEP members or their representatives shall visit the facility, interview personnel in charge of administering the experimental procedures, interview staff members of the facilities involved and residents taking part in the research and may seek PRC consultation to assure that no deviations in the approved protocols are occurring and that no participants appear to be in harm or danger as a consequence of the research. In addition, members of the PRC shall have authority to make on-site inspections if the PRC deems such visits to be advisable.

7.2 Interim Results

The interim results of a research study include the formal data collected by the investigators, reports made on the health status of the participants as part of the on-going operations of the involved facilities, and informal reports based on interviews with the participants, the staff of the facility, or the researchers.

7.3 Deviations from the Original Research Protocol

Variations in the administration of the research procedures should be spelled out in advance to the fullest extent feasible in the proposal. Thus, the conditions for increasing or decreasing or removing altogether the experimental procedures should be specified. Deviations in the protocol include the introduction of procedures not originally described, changes in the manner in which procedures were to be carried out, or the failure to use procedures described in the proposal. Deviations which pose harm or additional risk to the subjects shall be under the scrutiny of the CLEPs, while deviations which compromise the scientific integrity of the research shall be under the review of the PRC. Desired modifications which could not have been predicted but which may improve the project should be approved by the PRC and CLEP before implementation.

7.4 Appropriate Consequential Action

Upon finding that participants appear to be in increased jeopardy as a result of the research or that inappropriate deviations in the conduct of the research have occurred, the PRC and/or the CLEP shall intercede in the research to eliminate inappropriate deviations or to halt the research. In ordering a halt to or modification of the research procedure, the PRC or CLEP shall communicate its decision to the other reviewing body (the CLEP or PRC), the institution and the researcher, and may make on-site visits to the facility to assure that the project has been properly modified or halted. Failure of the researcher and facility to discontinue or to carry out the instructions of the CLEP or PRC shall constitute a basis for either reviewing body to seek a court injunction ordering the facility and researcher to comply with the instructions or to seek imposition of criminal or civil penalties.

8 *Enforcement Mechanisms*

Adequate enforcement measures shall exist for the protection of the participants.

8.1 Prevention of Abuses

The primary goal of these guidelines, as stated previously, is the prevention of the conditions under which abuses can occur. The means for achieving this goal is legislation and/or executive action establishing and funding professional review committees and state and local committees on legal and ethical protection. Such legislation or executive action would, of course, need to consider a number of additional factors, including federal requirements for review mechanisms, currently existing review structures and the on-going level of research in residential facilities. Of particular importance is the need to avoid intense bureaucratic arrangements and to coordinate the two major review functions, e.g., PRC and CLEP functions. Other matters should also be considered, such as the need for protection mechanisms in residential facilities beyond the research arena, the need for protection mechanisms in other kinds of residential facilities, and integrating the PRC and CLEP structures into existing state agencies.

8.1.1 Professional review committees. These groups shall enforce those portions of the guidelines dealing with the adequacy of the scientific merits of the study, its need, the adequacy of informed consent information, and the on-going review of the research methodology and its implementation. In addition, through input to a national registry to be described below, the PRC shall play a key role in maintaining a national data base on biomedical and pharmacological research.

8.1.2 Committees on legal and ethical protection. These groups, operating at state and local levels, shall be intimately involved in reviewing individual participants, supervising and evaluating the informed consent, supervising the health status of the subjects, ascertaining their competency and determining their continued willingness to participate. These groups shall have the power to stop research where they deem appropriate and to conduct investigational inquiries where adverse effects on participants are noted. The CLEP shall, by legislation, have access to all nonconfidential, pre-existing records of research participants. Legislation should be enacted spelling out the sanctions, fines and other consequences for the refusal to comply with a CLEP mandate or decision on the part of the researcher, the sponsor or the facility involved in the research.

The CLEP shall determine what proposals are to be approved, when subject selections may begin and when the research project itself may be initiated.

8.1.3 Project registration. A federal agency shall have responsibility for maintaining records of all research projects which are subject to FDA regulation, or receive federal funding, or which are conducted in institutions which receive federal funds. This registry shall be a public registry available for inspection. The agency shall supply copies of information in the registry upon request of interested parties.

Information to the registry shall be supplied by PRCs. Copies of reports on each proposal reviewed with the results of that review shall be supplied to the registry and become a permanent part of that record.

The PRC shall provide the bases for reviewing and rejecting, terminating or intervening in each research proposal or project. All official action by duly constituted bodies e.g., courts or review

commissions or administrative agencies relating to the research project shall similarly be made available to the registry.

The PRC shall also transmit to the registry a report of the CLEP review of and decisions made on proposals it has approved and forwarded to the PRC.

The PRC shall notify the registry of the termination of each project and the status at termination (e.g., whether or not the project was terminated prematurely and if so, by whom and for what reasons).

Failure to go through the PRC/CLEP review mechanism, or unauthorized deviation from the approved protocol, or failure to provide informed consent or to honor a request to withdraw by a participant shall be the bases for the PRC to initiate a grievance procedure. The basis for such actions shall be supplied to the federal registry. The grievance procedure may involve referral to an ethics committee of an appropriate professional group, a professional standard review organization (PSRO), or initiating civil or criminal complaint.

Each project shall be identified by the name and location of the researcher, sponsoring agency, type of research or treatment, duration of the project, the location where the study is being conducted, the number of participants, and the name and address of the appropriate PRC and CLEP. The reports on each project shall be maintained by the responsible agency in a manner such that data may be selected by any of the above identifiers and additional variables deemed useful by the agency.

8.1.4 Certification of facilities for research. Prior to the initiation of any research project, the appropriate federal and/or state supervisory or funding agency such as HEW, FDA, a permanent National Commission for the Protection of Human Subjects, or, in the absence of these, a state CLEP/PRC subcommittee shall conduct an on-site visit for the purpose of certifying facilities as an appropriate place for research to be conducted. This inspection shall determine that the facility meets the following criteria:

8.1.4.1 If the research shall take place in a hospital either within the residential facility or outside, it must have JCAH accreditation.

8.1.4.2 The residential facility has received AC/MR-DD accreditation.

8.1.4.3 The residential facility has a human rights committee.

8.1.4.4 There is a local CLEP as constituted in these guidelines. If the facility's human rights committee meets the requirements set forth for a CLEP, these need not be two separate bodies.

8.1.4.5 A duly constituted PRC exists.

8.1.4.6 Facilities meeting such requirements will be issued certification on an annual or some other periodic basis.

The local CLEP shall periodically review the certified facility to assure that the conditions met for the purpose of certification continue to be met throughout the project. In the event that these conditions are no longer met, the CLEP shall notify the certification agency and in turn the PRC shall notify the national project registry.

8.1.5 Insurance for research subjects. Every research project shall purchase insurance or certify obligation to protect its participants against any financial burdens arising from injury incurred by participation in the research. This is not malpractice insurance, but rather health, accident and injury insurance for the participants. Since liability for such financial burdens may also fall upon the facility where the research is carried out, the researcher should determine the extent to which the facility has insured against this sort of risk.

8.2 Sanctions

In the event that abuses and violations of the safeguards do occur, a number of sanctions are proposed in addition to that implicit in the previous discussion of a national registry of biomedical and pharmacological research projects. That the central registry will retain information on official actions related to review, suspension and termination of projects and instances of abuse, and that there will be free access to this information by interested parties constitute a clear deterrent to such abuses. Other sanctions may also be applied:

8.2.1 FDA clearance. The task force recommends strongly that the Food and Drug Administration adopt the following policy:

> Any data gathered in violation of the guidelines proposed herein shall be inadmissable documentation for FDA licensing. The sanction to be applied for violation of these safeguards is the denial of use of the data for clearance and licensing.

8.2.2 Professional group sanction. The PRC, at its own volition or at the request of a local or state CLEP, may contact grievance committees of appropriate professional organizations and request an investigation in cases of actual or suspected abuse for the purposes of applying sanctions to persons professionally responsible for such abuses.

8.2.3 Criminal or civil action. In extreme cases, the CLEP may seek civil court injunction to enforce its mandate or may contact the appropriate district attorney or state agency to register complaints or seek the initiation of criminal or other appropriate proceedings [see 2.5.4].

Conclusion

While some of the provisions in these guidelines may appear difficult, time consuming and bureaucratic, there is no intention to impose unnecessary hurdles but to prevent abuses. It is hoped that scientists, the PRCs and the CLEPs will not ordinarily be adversaries but will work cooperatively and practically for the conduct of research with the necessary precautions to protect human subjects.

The Association strongly supports and encourages the work of the nation's Mental Retardation Research Centers and independent researchers in universities and private foundations who are working to understand the causes of mental retardation, how to prevent it and ways to alleviate its impairing effects. It is hoped that future generations may be spared the burden of mental retardation through research leading to its prevention. At the same time, the humanity and value of all mentally retarded persons must be steadfastly bolstered and protected. It is to these dual goals that these guidelines are addressed.

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1978-79

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